

What is claimed is:

1. An isolated nucleic acid molecule which encodes a HICP protein, comprising a nucleotide sequence at least about 60% homologous to a nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3 or a complement thereof.

5 2. The isolated nucleic acid molecule of claim 1 comprising the nucleotide sequence of SEQ ID NO:1 or a complement thereof.

10 3. The isolated nucleic acid molecule of claim 2, further comprising nucleotides 1-883 of SEQ ID NO:1.

4. The isolated nucleic acid molecule of claim 2, further comprising nucleotides 1534-1708 of SEQ ID NO:1.

15 5. The isolated nucleic acid molecule of claim 1 comprising the nucleotide sequence of SEQ ID NO:3 or a complement thereof.

6. The isolated nucleic acid molecule of claim 5, further comprising 20 nucleotides 1-635 of SEQ ID NO:3.

7. The isolated nucleic acid molecule of claim 1 which specifically detects a HICP nucleic acid molecule relative to a nucleic acid molecule encoding a non-HICP protein.

25 8. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a protein which comprises an amino acid sequence at least about 60% homologous to the amino acid sequence of SEQ ID NO:2.

30 9. The isolated nucleic acid molecule of claim 8 comprising a nucleotide sequence encoding a protein which comprises the amino acid sequence of SEQ ID NO:2.

10. An isolated nucleic acid molecule encoding a HICP protein, comprising a nucleotide sequence which hybridizes under stringent hybridization conditions to a 35 nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3.

11. An isolated nucleic acid molecule comprising a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising nucleotides 1-883 of SEQ ID NO:1.

5 12. An isolated nucleic acid molecule at least 500 nucleotides in length which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3.

10 13. An isolated nucleic acid molecule which is at least about 60% homologous to a nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3 or a complement thereof, and encodes a polypeptide which has at least one of the following activities:

- 15 i) it can modulate cell proliferation;
ii) it can modulate a growth factor signaling pathway;
iii) it can modulate the activity of CTGF or PDGF; or
iv) it can modulate a heparin-induced response in a heparin-responsive cell.

14. The isolated nucleic acid molecule of claim 13 comprising the nucleotide sequence of SEQ ID NO:1 or a complement thereof.

20 15. The isolated nucleic acid molecule of claim 13 comprising the nucleotide sequence of SEQ ID NO:3 or a complement thereof.

16. An isolated nucleic acid molecule which is antisense to the nucleic acid molecule of any of claims 1, 9, 11 or 13.

25 17. A vector comprising the nucleic acid molecule of any of claims 1, 8, 10, or 13.

30 18. The vector of claim 17, which is a recombinant expression vector.

19. A host cell containing the vector of claim 18.

20. A method for producing HICP protein comprising culturing the host cell of claim 19 in a suitable medium until HICP protein is produced.

35 21. The method of claim 20, further comprising isolating HICP protein from the medium or the host cell.

22. A nonhuman transgenic animal which contains cells carrying a transgene encoding HICP protein.

23. A nonhuman homologous recombinant animal which contains cells
5 having an altered HICP gene.

24. An isolated HICP protein comprising an amino acid sequence at least about 60% homologous to the amino acid sequence of SEQ ID NO:2.

10 25. An isolated HICP protein which is encoded by a nucleic acid molecule comprising a nucleotide sequence at least about 60% homologous to a nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, or a complement thereof.

15 26. An isolated HICP protein which is encoded by a nucleic acid molecule comprising a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3.

20 27. An isolated HICP protein which is sufficiently homologous to the amino acid sequence of SEQ ID NO:2 and retains HICP biological activity.

28. The isolated protein of claim 27 comprising an amino acid sequence at least about 60% homologous to an amino acid sequence of SEQ ID NO:2.

25 29. An isolated HICP protein comprising an amino acid sequence at least about 60% homologous to the amino acid sequence of SEQ ID NO:2 and which has at least one of the following biological activities:

- i) it can modulate cell proliferation;
- ii) it can modulate a growth factor signaling pathway;
- 30 iii) it can modulate the activity of CTGF or PDGF;
- iv) it can modulate a heparin-induced response in a heparin-responsive cell;
- v) it can modulate cell motility; or
- vi) it can modulate extracellular matrix production.

35 30. The isolated protein of any of claims 24-29, comprising an N-terminal IGFBP motif.

31. The isolated protein of any of claims 24-29, comprising a VWC motif.

32. The isolated protein of any of claims 24-29, comprising a TSP1 motif.
33. An isolated protein comprising the amino acid sequence of SEQ ID
5 NO:2.
34. A fusion protein comprising a HICP polypeptide operatively linked to a non-HICP polypeptide.
- 10 35. An antibody that specifically binds HICP.
36. The antibody of claim 35, which is monoclonal.
37. The antibody of claim 36, which is labeled with a detectable substance.
- 15 38. A pharmaceutical composition comprising the protein of any one of claims 24-29, or 34, and a pharmaceutically acceptable carrier.
- 20 39. A pharmaceutical composition comprising the antibody of claim 35 and a pharmaceutically acceptable carrier.
- 25 40. A method for modulating a cell-associated activity comprising contacting a cell with an agent which modulates HICP protein activity or HICP nucleic acid expression such that the cell-associated activity is altered relative to the cell-associated activity of the cell in the absence of the agent.
41. The method of claim 40, wherein the agent stimulates a HICP protein activity or expression.
- 30 42. The method of claim 40, wherein the agent inhibits a HICP protein activity or expression.
43. The method of claim 42, wherein the agent is an antisense HICP nucleic acid molecule.
- 35 44. The method of claim 42, wherein the agent is an antibody that specifically binds to HICP.

45. The method of claim 40, wherein the cell is present within a subject and the agent is administered to the subject.

46. A method for treating a subject having a disorder characterized by 5 aberrant HICP protein activity or nucleic acid expression comprising administering to the subject a HICP modulator such that treatment of the subject occurs.

47. The method of claim 46 wherein the HICP modulator is a nucleic acid molecule encoding a HICP protein.

10 48. A method for detecting the presence of HICP activity in a biological sample comprising contacting a biological sample with an agent capable of detecting an indicator of HICP activity such that the presence of HICP activity is detected in the biological sample.

15 49. The method of claim 48, wherein the agent detects HICP mRNA.

50. The method of claim 49, wherein the agent is a labeled nucleic acid probe capable of hybridizing to HICP mRNA.

20 51. The method of claim 48, wherein the agent detects HICP protein.

52. The method of claim 48, wherein the agent is a labeled antibody capable of specifically binding to HICP protein.

25 53. A method for treating a disorder characterized by aberrant cell proliferation by administering to a subject having the disorder a HICP agent which alters cell proliferation relative to cell proliferation in the absence of the agent.

30 54. The method of claim 53, wherein the HICP agent is a HICP protein or portion thereof.

55. The method of claim 53, wherein the HICP agent is a nucleotide encoding a HICP protein.

35 56. The method of claim 53, wherein the disorder is a cardiovascular disorder.

57. The method of claim 53, wherein the disorder is a fibrotic disorder.
58. A diagnostic assay for identifying a genetic alteration in a cell sample, the presence or absence of the genetic alteration characterized by at least one of (i) aberrant 5 modification or mutation of a gene encoding a HICP protein, and (ii) mis-regulation of said gene or (iii) aberrant post-translational modification of a HICP protein.
59. The assay of claim 58, wherein detecting said alteration includes:
- 10 a. providing a reagent comprising a diagnostic probe of claim 11 or 12;
- b. combining said reagent with nucleic acid of said cell sample; and
- c. detecting, by hybridization of said probe to said cellular nucleic acid, the existence of at least one of a deletion of one or more nucleotides from said gene, an addition of one or more nucleotides to said gene, a substitution of one or more 15 nucleotides of said gene, a gross chromosomal rearrangement of all or a portion of said gene, a gross alteration in the level of an mRNA transcript of said gene, or a non-wild type splicing pattern of an mRNA transcript of said gene.
60. The assay of claim 58, wherein detecting said alteration includes:
- 20 a. providing a reagent comprising two diagnostic probes;
- b. combining said reagent with nucleic acid of said cell sample; and
- c. detecting, by amplification or lack of amplification of said cellular nucleic acid, the absence or existence of said alteration.
- 25 61. A method for isolating a heparin specie which has antiproliferative activity comprising:
- 30 a. contacting a HICP affinity reagent with a composition containing heparin species; and
- b. isolating the heparin specie which binds to the HICP affinity reagent to thereby obtain the heparin specie which has antiproliferative activity.